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| APPLICATION NO.                 | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---------------------------------|-------------|----------------------|---------------------|------------------|
| 10/659,711                      | 09/11/2003  | Carl R. Merrill      | NIH298.1DC1CC1      | 4758             |
| 20995                           | 7590        | 08/14/2007           | EXAMINER            |                  |
| KNOBBE MARTENS OLSON & BEAR LLP |             |                      | SNYDER, STUART      |                  |
| 2040 MAIN STREET                |             |                      | ART UNIT            | PAPER NUMBER     |
| FOURTEENTH FLOOR                |             |                      | 1648                |                  |
| IRVINE, CA 92614                |             |                      |                     |                  |
| NOTIFICATION DATE               |             | DELIVERY MODE        |                     |                  |
| 08/14/2007                      |             | ELECTRONIC           |                     |                  |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com  
eOAPilot@kmob.com

|                              |                  |               |
|------------------------------|------------------|---------------|
| <b>Office Action Summary</b> | Application No.  | Applicant(s)  |
|                              | 10/659,711       | MERRIL ET AL. |
|                              | Examiner         | Art Unit      |
|                              | Stuart W. Snyder | 1648          |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 21 June 2007.  
 2a) This action is FINAL.                            2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 20,22 and 23 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 20,22 and 23 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) Notice of References Cited (PTO-892)  
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)  
 3) Information Disclosure Statement(s) (PTO/SB/08)  
     Paper No(s)/Mail Date \_\_\_\_\_

4) Interview Summary (PTO-413)  
     Paper No(s)/Mail Date. \_\_\_\_\_

5) Notice of Informal Patent Application

6) Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/21/2007 has been entered.

Claims 20, 22, and 23 are pending and subject to examination

### ***Response to Arguments***

2. Applicant's arguments; see "Applicant Arguments/Remarks Made in an Amendment", filed 6/21/2007, with respect to the rejection(s) of claim(s) 20, 22, and 23 under 35 USC 112/1 Enablement have been fully considered and are not found to be persuasive. The Examiner explicitly acknowledges removal of the limitation "by inhibiting complement activation"; the arguments presented previously supporting rejection of the claims under 35 USC 112/1 and those below are not address to that limitation.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Art Unit: 1648

3. Claims 20, 22 and 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a method of producing bacteriophage able to delay inactivation by an animal's host defense system (HDS) comprising genetically engineering a bacteriophage to express molecules on its surface that delay inactivation of the bacteriophage by an animal's HDS, wherein the bacteriophage are lytic for certain named bacteria especially those of the genus *Mycobacterium* of the family *Mycobacteriaceae*.

The following facts are agreed upon by both the Examiner and Applicant: There is a profound need for effective treatments against existing and emerging pathogenic bacteria especially those that have acquired resistance against existing antimicrobials and development of bacteriophage as therapeutics seems a very promising route to accomplish this task. Applicants have succeeded in using one of three methods to produce a bacteriophage capable of increased circulation in an animal by serial passage of a "wild type" bacteriophage (Merril, et al. (1996)); subsequent investigation revealed a single point mutation of the phage genome resulting in a change in the amino acid sequence of a surface protein. More recently, Applicants have used certain molecular biological techniques available at the time of filing to insert a point mutation in a naturally

occurring surface protein of WT phage to obtain a phenotypic phage similar to that obtained through serial passage of WT phage in mice (Vitiello, et al. (2005)). Applicants have previously argued (see “Applicant Arguments/Remarks Made in an Amendment”, filed 2/20/2007) that using molecular biological techniques to recreate the virus obtained using the serial passage techniques constitutes the genetic engineering method prophetically described in the Specification and thus enables the claimed invention. Applicant further argues that the certain exemplified molecular biological techniques elaborated in the Specification were in fact used by the scientists of Dr. Merril’s laboratory, as taught by Vitiello, et al. as well as being attested to by Dr. Merril’s 37 CFR 1.132 Declaration.

The Examiner does not and has not disputed the factual evidence provided that molecular biological techniques were used to recreate the mutant phage. The Examiner has consistently maintained that the genetic engineering technique of Claim 20 is not equivalent to that either envisioned by the inventors or taught by the specification. Regarding interpretation of Claim 20, the Examiner has referenced MPEP 2111, excerpted below:

## **2111 [R-5] Claim Interpretation; Broadest Reasonable Interpretation**

### **CLAIMS MUST BE GIVEN THEIR BROADEST REASONABLE INTERPRETATION**

During patent examination, the pending claims must be “given their broadest reasonable interpretation consistent with the specification.” >The Federal Circuit’s *en banc* decision in *Phillips v. AWH Corp.*, 415 F.3d 1303, 75 USPQ2d 1321 (Fed. Cir. 2005) expressly recognized that the USPTO employs the “broadest reasonable interpretation” standard:

The Patent and Trademark Office (“PTO”) determines the scope of claims in patent applications not solely on the basis of the claim language, but upon giving claims their broadest reasonable construction “in light of the specification as it would be interpreted by one of ordinary skill in the art.” *In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364[, 70 USPQ2d 1827] (Fed. Cir. 2004). Indeed, the rules of the PTO require that application claims must “conform to the invention as set forth in the remainder of the specification and the terms and phrases used in the claims must find clear support or antecedent basis in the description so that the meaning of the terms in the claims may be ascertainable by reference to the description.” 37 CFR 1.75(d)(1).

The phrase relied upon by the Examiner to establish and maintain the rejection of the claims is “the genetic engineering technique”. Certainly, and there is no dispute between the Examiner and Applicants, the phrase encompasses certain delineated molecular biological techniques employed to create the bacteriophage taught in Vitiello, et al. However, the Specification further informs the Examiner as to the meaning of the phrase as contemplated by Applicants. Page 12 of the Specification reads, in part:

“An altogether different method to achieve the desired result is to genetically engineer a phage so that it expresses molecules on its surface coat, where said molecules **antagonize, inactivate, or in some other manner impede**

**those actions of the HDS that would otherwise reduce the viability of the administered phages."**

As taught by the specification, it is required that the genetic engineering technique result in a phage that impede actions of the HDS that would otherwise reduce viability of the phage. As previously asserted by the Examiner, no demonstration of involvement of the innate immune system in the mechanism of decrease in the number of circulating phage has been established and consequently no demonstration that the theorized involvement of the innate immune response has been compromised by the mutant phage. Also, in contrast to the methods explicitly taught by the specification to interfere with innate immunity, there is no literal teaching in the specification that describes introducing point mutations into naturally occurring phage coat proteins. Thus, the Examiner does not find Applicants' argument convincing that the method ultimately used, introducing a specific point mutation into the phage coat, was envisioned by Applicants at the time of filing.

Furthermore, although phage are not generally considered to be living entities, the term viability has an accepted meaning in the art, to wit, the replicative capacity of a phage. Viability has nothing to do with increased circulation in mammals, but solely the capacity of the phage to replicate in conducive environments. It is clear from a careful reading of Merril, et al. that the mutant phage originally obtained from serial passage was viable (see p. 3189-3190, results section entitled "Development and Partial Characterization of Long-

Circulating Bacteriophage") as evidenced by in vitro plaque formation and reduction of bacteria-induced disease. Direct evidence of decrease viability of phage is comparison of phage particles to plaque forming units. These experiments, well within the accepted and well-known array of virological techniques available in 1992, have not been performed to date.

The rejection of claims 20, 22 and 23 as lacking enablement in the specification is **maintained**.

4. Claims 20, 22 and 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to a method of making a broad genus of phages defined only by function. The only disclosed phage that has the function was not made by the claimed method and the specification does not provide enough information to permit one skilled in the art to recreate that species of phage by the method claimed. There is particular guidance to on species of phage (one displaying the peptide LARSLN) which could be made by the claimed generic method although not actually reduced to practice in the many intervening years since filing, but in regard to the genus as a whole there is little or no guidance as to which structures must be changed in the phages to obtain the desired function or how to change those features in order to obtain the desired function. There is no

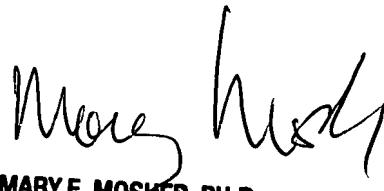
disclosed or previously recognized correlation between structural alterations and functional changes in inactivation by host defense systems. Considering the broad scope of the claims, the limited guidance in the specification, and the unpredictability of the art, it is concluded that the specification does not reasonably convey possession of the generic method now claimed.

***Conclusion***

5. No claims are allowed.
6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart W. Snyder whose telephone number is (571) 272-9945. The examiner can normally be reached on 9:00 AM-5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.  
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stuart W Snyder  
Examiner  
Art Unit 1648

sws



MARY E. MOSHER, PH.D.  
PRIMARY EXAMINER